

EXHIBIT A:

MOUSE LKB1 COMPARED TO HUMAN LKB1

BLAST

Basic Local Alignment Search Tool

[Edit and Resubmit](#) [Save Search Strategies](#) [Formatting options](#) [Download](#)

Blast 2 sequences

SEQ ID NO: 6 (44-343) Compared to Mouse LKB1

Results for:

Your BLAST job specified more than one input sequence. This box lets you choose which input sequence to show BLAST results for.

Query ID

[lc|41549](#)

[lc|41549](#)

Description

SEQ ID NO: 6

Molecule type

amino acid

Query Length

433

Subject ID

[gi|7106425|ref|NP_035622.1|](#)

Description

serine/threonine-protein kinase 11 [Mus musculus] >gi|81917862|sp|Q9WTK7.1|STK11_MOUSE RecName: Full=Serine/threonine-protein kinase 11; AltName: Full=Serine/threonine-protein kinase LKB1 >gi|4838565|gb|AAD31044.1|AF145287_1 Peutz-Jeghers syndrome kinase LKB1 [Mus musculus] >gi|6649101|gb|AAF21370.1|AF151711_1 protein kinase LKB1 [Mus musculus] >gi|4530575|gb|AAD22100.1| serine/threonine-protein kinase LKB1 [Mus musculus] >gi|4589404|dbj|BAA76749.1| LKB1 [Mus musculus] >gi|5901683|gb|AAD55368.1| Peutz-Jeghers syndrome protein [Mus musculus] >gi|30851173|gb|AAH52379.1| Serine/threonine kinase 11 [Mus musculus] >gi|74186437|dbj|BAE42977.1| unnamed protein product [Mus musculus] >gi|74192527|dbj|BAE43050.1| unnamed protein product [Mus musculus] >gi|117616790|gb|ABK42413.1| Stk11 [synthetic construct] >gi|148699653|gb|EDL31600.1| serine/threonine kinase 11, isoform CRA_a [Mus musculus]

Molecule type

amino acid

Subject Length

436

Program

BLASTP 2.2.24+ [Citation](#)

Reference

Stephen F. Altschul, Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

Reference - compositional score matrix adjustment

Stephen F. Altschul, John C. Wootton, E. Michael Gertz, Richa Agarwala, Aleksandr Morgulis, Alejandro A. Schäffer, and Yi-Kuo Yu (2005) "Protein database searches using compositionally adjusted substitution matrices", FEBS J. 272:5101-5109.

Other reports: [Search Summary](#) [Taxonomy reports](#) [Multiple alignment](#)

[Search Parameters](#)

Search parameter name Search parameter value

Program	blastp
Query range	44-343
Word size	3
Expect value	10
Hitlist size	100
Gapcosts	11,1
Matrix	BLOSUM62
Low Complexity Filter	Yes
Filter string	L;
Genetic Code	1
Window Size	40
Threshold	11
Composition-based stats	2

Karlin-Altschul statistics

Params Ungapped Gapped

Lambda	0.320459	0.267
K	0.139595	0.041
H	0.429592	0.14

Results Statistics

Results Statistics parameter name Results Statistics parameter value

Effective search space	110297
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Graphic Summary

Distribution of Blast Hits on the Query Sequence

[?]

An overview of the database sequences aligned to the query sequence is shown. The score of each alignment is indicated by one of five different colors, which divides the range of scores into five groups. Multiple alignments on the same database sequence are connected by a striped line. Mousing over a hit sequence causes the definition and score to be shown in the window at the top, clicking on a hit sequence takes the user to the associated alignments. New: This graphic is an overview of database sequences aligned to the query sequence. Alignments are color-coded by score, within one of five score ranges. Multiple alignments on the same database sequence are connected by a dashed line. Mousing over an alignment shows the alignment definition and score in the box at the top. Clicking an alignment displays the alignment detail.

[Dot Matrix View](#)**Plot of lcl|41549 vs gi|7106425|ref|NP_035622.1| [?]**

This dot matrix view shows regions of similarity based upon the BLAST results. The query sequence is represented on the X-axis and the numbers represent the bases/residues of the query. The subject is represented on the Y-axis and again the numbers represent the bases/residues of the subject. Alignments are shown in the plot as lines. Plus strand and protein matches are slanted from the bottom left to the upper right corner, minus strand matches are slanted from the upper left to the lower right. The number of lines shown in the plot is the same as the number of alignments found by BLAST.

**Descriptions**

Sequences producing significant alignments:	Score (Bits)	E Value
ref NP_035622.1 serine/threonine-protein kinase 11 [Mus musc...	526	4e-154

Alignments

```
>ref|NP_035622.1| serine/threonine-protein kinase 11 [Mus musculus]
sp|Q9WFK7.1|STK11_MOUSE RecName: Full=Serine/threonine-protein kinase 11; AltName: Full=Serine/threonine-protein kinase LKB1
gb|AAD31044.1|AF145287_1 Peutz-Jeghers syndrome kinase LKB1 [Mus musculus]
9 more sequence titles
```

```
gb|AAF21370.1|AF151711_1 protein kinase LKB1 [Mus musculus]
gb|AAD22100.1| serine/threonine-protein kinase LKB1 [Mus musculus]
db|BAA76749.1| LKB1 [Mus musculus]
gb|AAD55368.1| Peutz-Jeghers syndrome protein [Mus musculus]
gb|AAH52379.1| Serine/threonine kinase 11 [Mus musculus]
db|BAE42977.1| unnamed protein product [Mus musculus]
db|BAE43050.1| unnamed protein product [Mus musculus]
gb|ABK42413.1| Stk11 [synthetic construct]
gb|EDL31600.1| serine/threonine kinase 11, isoform CRA_a [Mus musculus]
Length=436
```

Score = 526 bits (1354), Expect = 4e-154, Method: Compositional matrix adjust.
Identities = 288/300 (96%), Positives = 292/300 (98%), Gaps = 0/300 (0%)

Query	44	KLIGKYLMDGLLGGESYGKVEVLDSSETLCRRAVKILKKKLRIPNGEANVKKEIQLLR	103
Sbjct	44	KLIGKYLMDGLLGGESYGKVEVLDSSETLCRRAVKILKKKLRIPNGEANVKKEIQLLR	103
Query	104	RLRHKNVIQLVDVLYNEEKQKMYMVMEYCVCGMQEMLDSVPEKRFPPVCAHGYFCQLIDG	163
Sbjct	104	RLRH+NVQLVDVLYNEEKQKMYMVMEYCVCGMQEMLDSVPEKRFPPVCAHGYF QLIDG	163
Query	164	LEYLHSQGIVHKDIKPGNLLTTGGTLKISDLGVAEALHPPFAADTCRTSQGSPAFQPPE	223
Sbjct	164	LEYLHSQGIVHKDIKPGNLLTTGTLKISDLGVAEALHPPFAADTCRTSQGSPAFQPPE	223
Query	224	IANGLDTFSGFKVDIWSAGVTLYNITGLYPFEGDNIYKLFENIGKGSYAIPGDCGPPLS	283
Sbjct	224	IANGLDTFSGFKVDIWSAGVTLYNITGLYPFEGDNIYKLFENIG+G + IP DCGPPLS	283
Query	284	DLLKGMLEYEPAKRFSIRQIRQHSWFRKKHppaeapvpippspDTKDRWRSMTVVPYLED	343
Sbjct	284	DLLRGMLEYEPAKRFSIRQIRQHSWFRKKHPLAEALVPIPPSPDTKDRWRSMTVVPYLED	343

EXHIBIT B:

MULTISPECIES COMPARISON OF STRAD POLYPEPTIDE

BLAST**Basic Local Alignment Search Tool**

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Blast 2 sequences

STRAD comparison

Results for:

Your BLAST job specified more than one input sequence. This box lets you choose which input sequence to show BLAST results for.

Query ID

[gi|51242955|ref|NP_001003787.1|](#)
[gi|51242955|ref|NP_001003787.1|](#)

Description

STE20-related kinase adapter protein alpha isoform 1 [Homo sapiens] >gi|74759034|sp|Q7RTN6.1|STRAA_HUMAN RecName: Full=STE20-related kinase adapter protein alpha; Short=STRAD alpha; AltName: Full=STE20-related adapter protein; AltName: Full=Serologically defined breast cancer antigen NY-BR-96 >gi|34494889|tpg|DAA01797.1| TPA_exp: STE20-related adaptor protein [Homo sapiens] >gi|119614691|gb|EAW94285.1| protein kinase LYK5, isoform CRA_c [Homo sapiens]

Molecule type

amino acid

Query Length

431

Subject ID

4 subjects

Description**Molecule type**

amino acid

Subject Length

n/a

Program

BLASTP 2.2.24+ [Citation](#)

Reference

Stephen F. Altschul, Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

Reference - compositional score matrix adjustment

Stephen F. Altschul, John C. Wootton, E. Michael Gertz, Richa Agarwala, Aleksandr Morgulis, Alejandro A. Schäffer, and Yi-Kuo Yu (2005) "Protein database searches using compositionally adjusted substitution matrices", FEBS J. 272:5101-5109.

Other reports: [Search Summary](#) [Taxonomy reports](#) [Distance tree of results](#) [Multiple alignment](#)

[Search Parameters](#)

Search parameter name Search parameter value

Program	blastp
Word size	3
Expect value	10
Hittlist size	100
Gapcosts	11,1
Matrix	BLOSUM62
Filter string	F
Genetic Code	1
Window Size	40
Threshold	11
Composition-based stats	2

Karlin-Altschul statistics

Params Ungapped Gapped

Lambda	0.318619	0.267
K	0.13404	0.041
H	0.398234	0.14

Results Statistics

Results Statistics parameter name Results Statistics parameter value

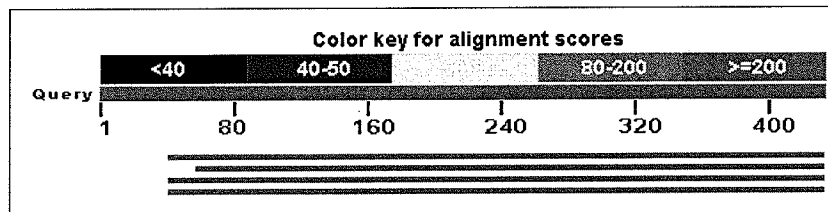
Effective search space	144800
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Graphic Summary

Distribution of 4 Blast Hits on the Query Sequence

[?]

An overview of the database sequences aligned to the query sequence is shown. The score of each alignment is indicated by one of five different colors, which divides the range of scores into five groups. Multiple alignments on the same database sequence are connected by a striped line. Mousing over a hit sequence causes the definition and score to be shown in the window at the top, clicking on a hit sequence takes the user to the associated alignments. New: This graphic is an overview of database sequences aligned to the query sequence. Alignments are color-coded by score, within one of five score ranges. Multiple alignments on the same database sequence are connected by a dashed line. Mousing over an alignment shows the alignment definition and score in the box at the top. Clicking an alignment displays the alignment detail.



Descriptions

Legend for links to other resources: [U](#) UniGene [E](#) GEO [G](#) Gene [S](#) Structure [M](#) Map Viewer [P](#) PubChem BioAssay
Sequences producing significant alignments:

Accession	Description	Max score	Total score	Query coverage	E value	Links
XP_850260.1	PREDICTED: similar to protein kinase LYK5 isoform 2 isoform 1 [Canis familiaris] STE20-related kinase adapter protein alpha [Bos taurus] >gi 240849233 ref NP_001155356.1 STE20-related kinase adapter protein alpha [Ovis aries] >gi 75070042 sp Q5E9J9.1 STRAA_BOVIN RecName: Full=STE20-related kinase adapter protein alpha; Short=STRAD alpha; AltName: Full=STE20-related adapter protein >gi 59858207 gb AA08938.1 protein kinase LYK5 isoform 4 [Bos taurus] >gi 238566930 gb ACR46653.1 STRADA [Ovis aries]	786	786	90%	0.0	UGM
NP_001015603.1	>gi 296476245 gb DAA18360.1 STE20-related kinase adapter protein alpha [Bos taurus] >ref NP_001155356.1 STE20-related kinase adapter protein alpha [Ovis aries] >sp Q5E9J9.1 STRAA_BOVIN RecName: Full=STE20-related kinase adapter protein alpha; Short=STRAD alpha; AltName: Full=STE20-related adapter protein >gb AA08938.1 protein kinase LYK5 isoform 4 [Bos taurus] >gb ACR46653.1 STRADA [Ovis aries] >gb DAA18360.1 STE20-related kinase adapter protein alpha [Bos taurus]	748	748	86%	0.0	UGM
NP_082402.1	STE20-related kinase adapter protein alpha [Mus musculus] >gi 12847582 dbj BAB27626.1 unnamed protein product [Mus musculus] >gi 33638094 gb AAQ24157.1 protein kinase LYK5 splice variant 1 [Mus musculus] >gi 35192984 gb AAH58517.1 RIKEN cDNA 2610019A05 gene [Mus musculus] >gi 117616946 gb ABK42491.1 STLK5 [synthetic construct] >gi 123243203 emb CAM27017.1 novel protein [Mus musculus] >gi 148702325 gb EDL34272.1 RIKEN cDNA 2610019A05, isoform CRA_b [Mus musculus] >gi 148702326 gb EDL34273.1 RIKEN cDNA 2610019A05, isoform CRA_b [Mus musculus] >dbj BAB27626.1 unnamed protein product [Mus musculus] >gb AAQ24157.1 protein kinase LYK5 splice variant 1 [Mus musculus] >gb AAH58517.1 RIKEN cDNA 2610019A05 gene [Mus musculus] >gb ABK42491.1 STLK5 [synthetic construct] >emb CAM27017.1 novel protein [Mus musculus] >gb EDL34272.1 RIKEN cDNA 2610019A05, isoform CRA_b [Mus musculus] >gb EDL34273.1 RIKEN cDNA 2610019A05, isoform CRA_b [Mus musculus]	775	775	90%	0.0	UGM
NP_877972.1	STE20-related kinase adapter protein alpha [Rattus norvegicus] >gi 81912054 sp Q7TNZ6.1 STRAA_RAT RecName: Full=STE20-related kinase adapter protein alpha; Short=STRAD alpha; AltName: Full=STE20-related adapter protein >gi 33087213 gb AAP92801.1 protein kinase LYK5 [Rattus norvegicus] >sp Q7TNZ6.1 STRAA_RAT RecName: Full=STE20-related kinase adapter protein alpha; Short=STRAD alpha; AltName: Full=STE20-related adapter protein >gb AAP92801.1 protein kinase LYK5 [Rattus norvegicus]	758	758	90%	0.0	UGM

Alignments

Select All [Get selected sequences](#) [Distance tree of results](#) [Multiple alignment](#)

>ref|[XP_850260.1](#)| [UGM](#) PREDICTED: similar to protein kinase LYK5 isoform 2 isoform 1 [Canis familiaris]
Length=394

GENE ID: 609377 STRADA | STE20-related kinase adaptor alpha
[Canis lupus familiaris]

Score = 786 bits (2030), Expect = 0.0, Method: Compositional matrix adjust.
Identities = 376/390 (97%), Positives = 381/390 (98%), Gaps = 0/390 (0%)

Query	42	TNDASSESIASFQKQEVMSFLPEGGCYELLTVIGKGFEDLMTVNLARYKPTGEYVTVRR	101
Sbjct	5	TNEASSESIASLSKQEIIMSSFLPEGGRYELLTIIGKGFEDLMTVNLARYKPTGEYVTVRR	64
Query	102	INLEACSNEMVTFQLQGLHVSCLFNHPNIPYRATFIADNELWVVTSPMAYGSAKDLICT	161
Sbjct	65	INLEACSNEMVTFQLQGLHVSCLFHPNIPYRATFIADNELWVVTSPMAYGSAKDLICT	124
Query	162	HFMDGMNELAIAYILQGVKLALDYIHHMGVYHRSVKASHILISVDGKVYLSGLRSLNLSMI	221
Sbjct	125	HFMDGMNELAIAYILQGVKLALDYIHHMGVYHRSVKASHILISSDGKVYLSGLRSLNLSMI	184
Query	222	SHGQRQRVVHDFPKYSVKVLPWLSPEVLQQLQGYDAKSDIYSGVITACELANGHVFPKD	281
Sbjct	185	SHGQRQRVVHDFPKYSVKVLPWLSPEVLQQLQGYDAKSDIYSGVITACELANGHVFPKD	244
Query	282	MPATQMLLEKLNLTVPCLLDSTIPAEELTMSPSRSVANSGLSDSLTSTTPRPSNGDSPS	341
Sbjct	245	MPATQMLLEKLNLTVPCLLDSTIPAEELTMSRSANSGLSDSLTSTTPRPSNGDSPS	304
Query	342	HPYHRTFSPHFHHFVEQCLQRNPDPARPSASTLLNHSFFKQIKRRASEALPELLRPVTPIT	401
Sbjct	305	HPYHRTFSPHFHHFVEQCLQRNPDPARPSASTLLNHSFFKQIKRRASEALPELLRPVTPIT	364
Query	402	NFEQSQSQDHSGIFGLVTNLEELEVDWDF 431	
		NFEQSQ QDHSGIFGLVTNLEELEVDWDF	

Sbjct 365 NFEQSQPQDHSGIFGLVTNLEELEVDWDEF 394

>ref|NP_001015603.1| **UGM** STE20-related kinase adapter protein alpha [Bos taurus]
 ref|NP_001155356.1| **UG** STE20-related kinase adapter protein alpha [Ovis aries]
 sp|Q5E9J9.1|STRAA_BOVIN **G** RecName: Full=STE20-related kinase adapter protein alpha; Short=STRAD
 alpha; AltName: Full=STE20-related adapter protein
 gb|AA08938.1| **G** protein kinase LYK5 isoform 4 [Bos taurus]
 gb|ACR46653.1| **G** STRADA [Ovis aries]
 gb|DAA18360.1| **G** STE20-related kinase adapter protein alpha [Bos taurus]
 Length=373

GENE ID: 515024 STRADA | STE20-related kinase adaptor alpha [Bos taurus]
 (10 or fewer PubMed links)

Score = 748 bits (1932), Expect = 0.0, Method: Compositional matrix adjust.
 Identities = 356/373 (96%), Positives = 362/373 (98%), Gaps = 0/373 (0%)

Query	59	MSSFLPEGGCYELLTVIGKGFEDLMTVNLARYKPTGEYVTVRRINLEACSNEMVTFLQGE	118
Sbjct	1	MSSFLPEGGCYELLTVIGKGFEDLMTVNLARYKPTGEYVTVRRINLEACSNEMVTFLQGE	60
Query	119	LHVSXLFNHPNIVPYRATFIADNELWVVTSMAYGSAKDLCITHFMDGMNELAIAYILQG	178
Sbjct	61	LHVSXLFNHPNIVPYRATFIADNELWVVTSMAYGSAKDLCITHFMDGMNELAIAYILQG	120
Query	179	VLKALDYIHHMGYVHRSVKASHILISVDGKVYLSGLRSNLSMISHGQRQVRVHDFPKYSV	238
Sbjct	121	ALKALDYIHHMGYVHRSVKASHILISADGKVYLSGLRSNLSMISHGQRQVRVHDFPKYSI	180
Query	239	KVLPWLSPEVLQONLQGYDAKSDIYSGITACELANGHVFPKDMPATQMLEKLNQTVPC	298
Sbjct	181	KVLPWLSPEVLQONLQGYDAKSDIYSGITACELANGHVFPKDMPATQMLEKLNQTVPC	240
Query	299	LLDTSTIPAEELTMSPSRSVANSGLSDSLTTSTPRPSNGDSPSHPHYRTFSPHFHHFVEQ	358
Sbjct	241	LLDTSTIPAEELTMSPSRSVANSGLSDSLTTSTPRPSNGDSPSHPHYRTFSPHFHHFVEQ	300
Query	359	CLQRNPDARPSASTLLNHSFFKQIKRRASEALPELLRPVTPITNFEQSQSQDHSGIFGLV	418
Sbjct	301	CLQRNPDARPSASTLLNHSFFKQIKRRASEALPELLRPVTPITNFEQSQSQDHSGIFGLV	360
Query	419	TNLEELEVDWDEF	431
Sbjct	361	TNLEELEVDWDEF	373

>ref|NP_082402.1| **UGM** STE20-related kinase adapter protein alpha [Mus musculus]
 dbj|BAB27626.1| **G** unnamed protein product [Mus musculus]
 gb|AAQ24157.1| **G** protein kinase LYK5 splice variant 1 [Mus musculus]
 gb|AAH58517.1| **G** RIKEN cDNA 2610019A05 gene [Mus musculus]
 gb|ABK42491.1| **G** STLK5 [synthetic construct]
 emb|CAM27017.1| **G** novel protein [Mus musculus]
 gb|EDL34272.1| **G** RIKEN cDNA 2610019A05, isoform CRA_b [Mus musculus]
 gb|EDL34273.1| **G** RIKEN cDNA 2610019A05, isoform CRA_b [Mus musculus]
 Length=394

GENE ID: 72149 Strada | STE20-related kinase adaptor alpha [Mus musculus]
 (Over 10 PubMed links)

Score = 775 bits (2001), Expect = 0.0, Method: Compositional matrix adjust.
 Identities = 369/390 (95%), Positives = 380/390 (98%), Gaps = 0/390 (0%)

Query	42	TNDASSESIASFQSKQEVMSFLPEGGCYELLTVIGKGFEDLMTVNLARYKPTGEYVTVRR	101
Sbjct	5	ANEASSESIASFQSKPEMMSFLPEGGCYELLTVIGKGFEDLMTVNLARYKPTGEYVTVRR	64
Query	102	INLEACSNEMVTFLQGEHVSKLFPNIVPYRATFIADNELWVVTSMAYGSAKDLCIT	161
Sbjct	65	INLEACSNEMVTFLQGEHVSKLFPNIVPYRATFIADNELWVVTSMAYGSAKDLCIT	124
Query	162	HFMDGMNELAIAYILQGVKALDYIHHMGYVHRSVKASHILISVDGKVYLSGLRSNLSMI	221
Sbjct	125	HFMDGMNELAIAYILQGVKALDYIHHMGYVHRSVKASHILISVDGKVYLSGLRSNLSMI	184
Query	222	SHGQRQVRVHDFPKYSVSVLPWLSPEVLQONLQGYDAKSDIYSGITACELANGHVFPKD	281
Sbjct	185	SHGQRQVRVHDFPKYSVSVLPWLSPEVLQONLQGYDAKSDIYSGITACELANGHVFPKD	244
Query	282	MPATQMLEKLNQTVPCLLDTSTIPAEELTMSPSRSVANSGLSDSLTTSTPRPSNGDSPS	341
Sbjct	245	MPATQMLEKLNQTVPCLLDTSTIPAEELTMSPSRSVANSGLSDSLTTSTPRPSNGDSPS	304
Query	342	HPYHRTFSPHFHHFVEQCLQRNPDARPSASTLLNHSFFKQIKRRASEALPELLRPVTPIT	401
Sbjct	305	HPYHRTFSPHFHHFVEQCLQRNPDARPSASTLLNHSFFKQIKRRASEALPELLRPVTPIT	364
Query	402	NFEQSQSQDHSGIFGLVTNLEELEVDWDEF	431
Sbjct	365	NFEQSQSQDHSGIFGLVTNLEELEVDWDEF	394

>ref|NP_877972.1| **UGM** STE20-related kinase adapter protein alpha [Rattus norvegicus]
 sp|Q7TNZ6.1|STRAA_RAT **G** RecName: Full=STE20-related kinase adapter protein alpha; Short=STRAD
 alpha; AltName: Full=STE20-related adapter protein
 gb|AAP92801.1| **G** protein kinase LYK5 [Rattus norvegicus]
 Length=393

GENE ID: 303605 Strada | STE20-related kinase adaptor alpha [Rattus norvegicus]
 (10 or fewer PubMed links)

Score = 758 bits (1958), Expect = 0.0, Method: Compositional matrix adjust.
 Identities = 362/390 (93%), Positives = 377/390 (97%), Gaps = 1/390 (0%)

Query	42	TNDASSESIASFQKQEVMSFLPEGGCYELLTVIGKGFEDLMTVNLARYKPTGEYVTVRR	101
		N+ASSESIASFQK E+MSSFLPEGGCYELL+VIGKGFEDLMTVN +RYKPTGEYVTVRR	
Sbjct	5	ANEASSESIASFQKPEIMSSFLPEGGCYELLSVIGKGFEDLMTVN- SRYKPTGEYVTVRR	63
Query	102	INLEACSNEMVTFLQGELHVSCLFNHPNIVPYRATFIADNELWVTSFMAYGSAKDLICT	161
		INLEACSNEMVTFLQGELHVSCLF+HPNIVPYRATFIADNELW VTSFMAYGSAKDLI T	
Sbjct	64	INLEACSNEMVTFLQGELHVSCLFHPNIVPYRATFIADNELWAVTSFMAYGSAKDLIGT	123
Query	162	HFMDGMNELAIAYILQGVKALDYIHHMGVYVHRSVKASHILISVDGKVYLSGLRSNLSMI	221
		HFMDGM+ELAIAYILQGVKALDYIHHMGVYVHRSVKASHILIS DGKVYLSGLRSNLSMI	
Sbjct	124	HFMDGMSELAIAYILQGVKALDYIHHMGVYVHRSVKASHILISTDGKVYLSGLRSNLSMI	183
Query	222	SHGQRQRVVHDFPKYSVKVLPWLSPEVLQQLQGYDAKSDIYSVGITACELANGHVPFKD	281
		SHGQRQRVHDFPKYS+KVLPLWLSPEVLQQLQGYDAKSDIYSVGITACELANGHVPFKD	
Sbjct	184	SHGQRQRAVHDFPKYSIKVLPWLSPEVLQQLQGYDAKSDIYSVGITACELANGHVPFKD	243
Query	282	MPATQMLLEKLNQTVPCLLDTSTIPAEELTMSPSRSVANSGLSDSLTSTPRPSNGDSPS	341
		MPATQMLLEKLNQTVPCLLDTSTIPAEELTMSPSR+AN GL+DSL + RP+NGDSPS	
Sbjct	244	MPATQMLLEKLNQTVPCLLDTSTIPAEELTMSPSRSIANPGLNDSLAAAGSLRPANGDSPS	303
Query	342	HPYHRTFSPHFFHFVEQCLQRNPDPASASTLLNHSFFKQIKRRASEALPELLRPVTPIT	401
		HPYHRTFSPHFFH+FVEQCLQRNPDPAP+ASTLLNHSFFKQIKRRASEALPELLRPVTPIT	
Sbjct	304	HPYHRTFSPHFFHFVEQCLQRNPDPAPNASTLLNHSFFKQIKRRASEALPELLRPVTPIT	363
Query	402	NFEGSQSQDHSGIFGLVTNLEEELEVDWDF	431
		+FEGSQSQDHSGI GLVTNLE+LEVDDWDF	
Sbjct	364	SFEGSQSQDHSGILGLVTNLEDELEVDDWDF	393

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EXHIBIT C:

MULTISPECIES COMPARISON OF MO25 POLYPEPTIDE


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☐ 1: HomoloGene:69212. Gene conserved in Eukaryota

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Pairwise Alignment Scores

Gene		Identity (%)		Substitution Rates ¹			
Species	Symbol	Protein	DNA	d	d _N /d _S	d _{NR} /d _{NC}	
Homo sapiens		CAB39					
vs. Pan troglodytes	CAB39	100.0	99.9	0.001	0	0	Blast
vs. Canis lupus familiaris	CAB39	99.4	94.8	0.054	0	0	Blast
vs. Bos taurus	CAB39	100.0	94.0	0.062	0	0	Blast
vs. Mus musculus	Cab39	98.8	92.4	0.080	0	0	Blast
vs. Rattus norvegicus	Cab39	99.4	92.6	0.078	0	0	Blast
vs. Danio rerio	cab39	93.0	79.6	0.239	0	0	Blast
vs. Drosophila melanogaster	Mo25	71.9	63.8	0.494	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP000812	72.6	64.1	0.489	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP011060	73.3	64.8	0.476	0	0	Blast
vs. Caenorhabditis elegans	mop-25.1	65.3	61.7	0.537	0	0	Blast
vs. Caenorhabditis elegans	mop-25.2	61.2	60.5	0.561	0	0	Blast
vs. Schizosaccharomyces pombe	pmo25	51.7	55.7	0.669	0	0	Blast
vs. Arabidopsis thaliana	AT4G17270	44.7	52.4	0.756	0	0	Blast
vs. Arabidopsis thaliana	AT5G47540	43.5	52.5	0.753	0	0	Blast
vs. Oryza sativa	Os07g0585100	47.0	54.1	0.711	0	0	Blast
Pan troglodytes		CAB39					
vs. Homo sapiens	CAB39	100.0	99.9	0.001	0	0	Blast
vs. Canis lupus familiaris	CAB39	99.4	94.8	0.054	0	0	Blast
vs. Bos taurus	CAB39	100.0	93.9	0.063	0	0	Blast
vs. Mus musculus	Cab39	98.8	92.3	0.081	0	0	Blast
vs. Rattus norvegicus	Cab39	99.4	92.5	0.079	0	0	Blast
vs. Danio rerio	cab39	93.0	79.6	0.239	0	0	Blast
vs. Drosophila melanogaster	Mo25	71.9	63.8	0.494	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP000812	72.6	64.1	0.489	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP011060	73.3	64.8	0.476	0	0	Blast
vs. Caenorhabditis elegans	mop-25.1	65.3	61.7	0.537	0	0	Blast
vs. Caenorhabditis elegans	mop-25.2	61.2	60.5	0.561	0	0	Blast
vs. Schizosaccharomyces pombe	pmo25	51.7	55.6	0.672	0	0	Blast
vs. Arabidopsis thaliana	AT4G17270	44.7	52.4	0.756	0	0	Blast
vs. Arabidopsis thaliana	AT5G47540	43.5	52.5	0.753	0	0	Blast
vs. Oryza sativa	Os07g0585100	47.0	54.1	0.711	0	0	Blast
Canis lupus familiaris		CAB39					
vs. Homo sapiens	CAB39	99.4	94.8	0.054	0	0	Blast
vs. Pan troglodytes	CAB39	99.4	94.8	0.054	0	0	Blast
vs. Bos taurus	CAB39	99.4	93.5	0.067	0	0	Blast
vs. Mus musculus	Cab39	98.8	91.2	0.094	0	0	Blast

vs. <i>Rattus norvegicus</i>	Cab39	99.4	91.4	0.091	0	0	Blast
vs. <i>Danio rerio</i>	cab39	93.0	79.6	0.239	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	72.5	64.5	0.480	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	72.9	64.5	0.482	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	73.6	64.9	0.474	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	65.3	61.1	0.549	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	60.9	60.3	0.565	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	54.5	0.700	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	44.7	52.1	0.764	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.5	52.1	0.764	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	47.0	54.1	0.711	0	0	Blast
Bos taurus		CAB39					
vs. <i>Homo sapiens</i>	CAB39	100.0	94.0	0.062	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	100.0	93.9	0.063	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	99.4	93.5	0.067	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	98.8	91.6	0.089	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	99.4	92.0	0.085	0	0	Blast
vs. <i>Danio rerio</i>	cab39	93.0	79.4	0.241	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	71.9	65.7	0.458	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	72.6	65.4	0.465	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	73.3	66.2	0.450	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	65.3	61.7	0.537	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	61.2	60.6	0.559	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	53.8	0.718	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	44.7	52.1	0.764	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.5	52.5	0.753	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	47.0	54.5	0.701	0	0	Blast
Mus musculus		Cab39					
vs. <i>Homo sapiens</i>	CAB39	98.8	92.4	0.080	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	98.8	92.3	0.081	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	98.8	91.2	0.094	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	98.8	91.6	0.089	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	99.4	96.4	0.037	0	0	Blast
vs. <i>Danio rerio</i>	cab39	92.4	80.4	0.227	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	72.2	66.5	0.445	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	72.9	66.4	0.446	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	72.6	66.6	0.443	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	64.3	61.4	0.543	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	61.2	59.6	0.580	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	54.0	0.713	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	45.0	53.1	0.737	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.5	51.7	0.775	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	47.0	53.9	0.716	0	0	Blast
Rattus norvegicus		Cab39					
vs. <i>Homo sapiens</i>	CAB39	99.4	92.6	0.078	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	99.4	92.5	0.079	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	99.4	91.4	0.091	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	99.4	92.0	0.085	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	99.4	96.4	0.037	0	0	Blast
vs. <i>Danio rerio</i>	cab39	93.0	80.0	0.233	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	72.2	65.7	0.458	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	72.9	66.0	0.454	0	0	Blast

vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	72.6	65.9	0.455	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	64.3	61.2	0.547	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	61.2	59.8	0.576	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	53.7	0.720	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	44.7	52.2	0.761	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.5	51.5	0.781	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	47.0	54.2	0.708	0	0	Blast
Danio rerio	cab39						
vs. <i>Homo sapiens</i>	CAB39	93.0	79.6	0.239	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	93.0	79.6	0.239	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	93.0	79.6	0.239	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	93.0	79.4	0.241	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	92.4	80.4	0.227	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	93.0	80.0	0.233	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	69.5	68.8	0.404	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	70.9	69.4	0.393	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	70.6	67.8	0.421	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	63.8	62.1	0.529	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	60.9	61.1	0.548	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	52.5	0.753	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	45.3	53.2	0.734	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.8	52.1	0.764	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	47.0	53.7	0.722	0	0	Blast
Drosophila melanogaster	Mo25						
vs. <i>Homo sapiens</i>	CAB39	71.9	63.8	0.494	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	71.9	63.8	0.494	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	72.5	64.5	0.480	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	71.9	65.7	0.458	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	72.2	66.5	0.445	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	72.2	65.7	0.458	0	0	Blast
vs. <i>Danio rerio</i>	cab39	69.5	68.8	0.404	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	88.7	82.2	0.203	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	86.4	82.5	0.199	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	65.8	64.3	0.485	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	63.5	59.8	0.576	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	52.1	51.1	0.791	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	42.4	51.3	0.785	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	42.1	50.2	0.818	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	46.2	52.3	0.758	0	0	Blast
Anopheles gambiae	AgaP_AGAP000812						
vs. <i>Homo sapiens</i>	CAB39	72.6	64.1	0.489	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	72.6	64.1	0.489	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	72.9	64.5	0.482	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	72.6	65.4	0.465	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	72.9	66.4	0.446	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	72.9	66.0	0.454	0	0	Blast
vs. <i>Danio rerio</i>	cab39	70.9	69.4	0.393	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	88.7	82.2	0.203	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	93.7	90.7	0.100	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	66.2	64.9	0.474	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	62.0	61.8	0.534	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	50.9	50.1	0.821	0	0	Blast

vs. <i>Arabidopsis thaliana</i>	AT4G17270	43.1	51.1	0.793	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.3	49.8	0.830	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	46.0	51.6	0.776	0	0	Blast
Anopheles gambiae	AgaP_AGAP011060						
vs. <i>Homo sapiens</i>	CAB39	73.3	64.8	0.476	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	73.3	64.8	0.476	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	73.6	64.9	0.474	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	73.3	66.2	0.450	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	72.6	66.6	0.443	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	72.6	65.9	0.455	0	0	Blast
vs. <i>Danio rerio</i>	cab39	70.6	67.8	0.421	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	86.4	82.5	0.199	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	93.7	90.7	0.100	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	63.5	65.4	0.464	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	60.5	60.5	0.561	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	50.6	50.0	0.824	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	43.1	50.6	0.807	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	42.9	48.5	0.869	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	44.8	50.8	0.800	0	0	Blast
Caenorhabditis elegans	mop-25.1						
vs. <i>Homo sapiens</i>	CAB39	65.3	61.7	0.537	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	65.3	61.7	0.537	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	65.3	61.1	0.549	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	65.3	61.7	0.537	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	64.3	61.4	0.543	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	64.3	61.2	0.547	0	0	Blast
vs. <i>Danio rerio</i>	cab39	63.8	62.1	0.529	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	65.8	64.3	0.485	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	66.2	64.9	0.474	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	63.5	65.4	0.464	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	72.1	66.2	0.450	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	53.3	0.731	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	45.5	50.8	0.800	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	46.5	50.1	0.822	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	48.5	52.7	0.747	0	0	Blast
Caenorhabditis elegans	mop-25.2						
vs. <i>Homo sapiens</i>	CAB39	61.2	60.5	0.561	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	61.2	60.5	0.561	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	60.9	60.3	0.565	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	61.2	60.6	0.559	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	61.2	59.6	0.580	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	61.2	59.8	0.576	0	0	Blast
vs. <i>Danio rerio</i>	cab39	60.9	61.1	0.548	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	63.5	59.8	0.576	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	62.0	61.8	0.534	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	60.5	60.5	0.561	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	72.1	66.2	0.450	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	48.8	52.0	0.765	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	42.9	49.5	0.839	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	42.2	49.9	0.827	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	45.5	51.2	0.789	0	0	Blast
Schizosaccharomyces pombe	pmo25						

vs. Homo sapiens	CAB39	51.7	55.7	0.669	0	0	Blast
vs. Pan troglodytes	CAB39	51.7	55.6	0.672	0	0	Blast
vs. Canis lupus familiaris	CAB39	51.7	54.5	0.700	0	0	Blast
vs. Bos taurus	CAB39	51.7	53.8	0.718	0	0	Blast
vs. Mus musculus	Cab39	51.7	54.0	0.713	0	0	Blast
vs. Rattus norvegicus	Cab39	51.7	53.7	0.720	0	0	Blast
vs. Danio rerio	cab39	51.7	52.5	0.753	0	0	Blast
vs. Drosophila melanogaster	Mo25	52.1	51.1	0.791	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP000812	50.9	50.1	0.821	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP011060	50.6	50.0	0.824	0	0	Blast
vs. Caenorhabditis elegans	mop-25.1	51.7	53.3	0.731	0	0	Blast
vs. Caenorhabditis elegans	mop-25.2	48.8	52.0	0.765	0	0	Blast
vs. Arabidopsis thaliana	AT4G17270	39.9	51.0	0.794	0	0	Blast
vs. Arabidopsis thaliana	AT5G47540	40.4	50.3	0.816	0	0	Blast
vs. Oryza sativa	Os07g0585100	43.0	51.4	0.782	0	0	Blast
Arabidopsis thaliana		AT4G17270					
vs. Homo sapiens	CAB39	44.7	52.4	0.756	0	0	Blast
vs. Pan troglodytes	CAB39	44.7	52.4	0.756	0	0	Blast
vs. Canis lupus familiaris	CAB39	44.7	52.1	0.764	0	0	Blast
vs. Bos taurus	CAB39	44.7	52.1	0.764	0	0	Blast
vs. Mus musculus	Cab39	45.0	53.1	0.737	0	0	Blast
vs. Rattus norvegicus	Cab39	44.7	52.2	0.761	0	0	Blast
vs. Danio rerio	cab39	45.3	53.2	0.734	0	0	Blast
vs. Drosophila melanogaster	Mo25	42.4	51.3	0.785	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP000812	43.1	51.1	0.793	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP011060	43.1	50.6	0.807	0	0	Blast
vs. Caenorhabditis elegans	mop-25.1	45.5	50.8	0.800	0	0	Blast
vs. Caenorhabditis elegans	mop-25.2	42.9	49.5	0.839	0	0	Blast
vs. Schizosaccharomyces pombe	pmo25	39.9	51.0	0.794	0	0	Blast
vs. Arabidopsis thaliana	AT5G47540	87.2	85.4	0.162	0	0	Blast
vs. Oryza sativa	Os07g0585100	70.8	70.5	0.374	0	0	Blast
Arabidopsis thaliana		AT5G47540					
vs. Homo sapiens	CAB39	43.5	52.5	0.753	0	0	Blast
vs. Pan troglodytes	CAB39	43.5	52.5	0.753	0	0	Blast
vs. Canis lupus familiaris	CAB39	43.5	52.1	0.764	0	0	Blast
vs. Bos taurus	CAB39	43.5	52.5	0.753	0	0	Blast
vs. Mus musculus	Cab39	43.5	51.7	0.775	0	0	Blast
vs. Rattus norvegicus	Cab39	43.5	51.5	0.781	0	0	Blast
vs. Danio rerio	cab39	43.8	52.1	0.764	0	0	Blast
vs. Drosophila melanogaster	Mo25	42.1	50.2	0.818	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP000812	43.3	49.8	0.830	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP011060	42.9	48.5	0.869	0	0	Blast
vs. Caenorhabditis elegans	mop-25.1	46.5	50.1	0.822	0	0	Blast
vs. Caenorhabditis elegans	mop-25.2	42.2	49.9	0.827	0	0	Blast
vs. Schizosaccharomyces pombe	pmo25	40.4	50.3	0.816	0	0	Blast
vs. Arabidopsis thaliana	AT4G17270	87.2	85.4	0.162	0	0	Blast
vs. Oryza sativa	Os07g0585100	76.5	72.1	0.349	0	0	Blast
Oryza sativa		Os07g0585100					
vs. Homo sapiens	CAB39	47.0	54.1	0.711	0	0	Blast
vs. Pan troglodytes	CAB39	47.0	54.1	0.711	0	0	Blast
vs. Canis lupus familiaris	CAB39	47.0	54.1	0.711	0	0	Blast
vs. Bos taurus	CAB39	47.0	54.5	0.701	0	0	Blast

vs. <i>Mus musculus</i>	Cab39	47.0	53.9	0.716	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	47.0	54.2	0.708	0	0	Blast
vs. <i>Danio rerio</i>	cab39	47.0	53.7	0.722	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	46.2	52.3	0.758	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	46.0	51.6	0.776	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	44.8	50.8	0.800	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	48.5	52.7	0.747	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	45.5	51.2	0.789	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	43.0	51.4	0.782	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	70.8	70.5	0.374	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	76.5	72.1	0.349	0	0	Blast

¹ We present three rates for nucleotide substitutions per site, as defined below:

- **d**: the number of nucleotide substitutions per site, corrected for multiple substitutions using the method of Jukes and Cantor (1969).
- **d_N/d_S** : the ratio of the rate of nonsynonymous substitutions (d_N) to the rate of synonymous substitutions (d_S), calculated using the method of Nei and Gojobori (1986). A high value of this metric indicates adaptive selection, whereas a low value indicates purifying selection.
- **d_{NR}/d_{NC}** : the ratio of radical nonsynonymous substitutions (d_{NR}) to conservative nonsynonymous substitutions (d_{NC}), calculated using the method of Hughes et al. (1990). This metric is analogous to d_N/d_S , but it has the advantage of being useful for studying the evolution of sequences that diverged in the distant past.

References

- Jukes TH, Cantor CR. Evolution of protein molecules. In: HN Munro, editor. Mammalian protein metabolism III. New York: Academic Press; 1969. p.21-132.
- Nei M, Gojobori T. Simple methods for estimating the numbers of synonymous and nonsynonymous nucleotide substitutions. Mol Biol Evol. 1986;3(5):418-26.
- Hughes AL, Ota T, Nei M. Positive Darwinian selection promotes charge profile diversity in the antigen-binding cleft of class I MHC molecules. Mol Biol Evol. 1990;7(6):515-24.

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EXHIBIT D:


COMPARISON OF RAT AND HUMAN LKB1

BLAST**Basic Local Alignment Search Tool**

[Edit and Resubmit](#) [Save Search Strategies](#) [Formatting options](#) [Download](#)

Blast 2 sequences

SEQ ID NO: 6

Results for: 

Your BLAST job specified more than one input sequence. This box lets you choose which input sequence to show BLAST results for.

Query ID

[lcl|17777](#)

[lcl|17777](#)

Description

SEQ ID NO: 6

Molecule type

amino acid

Query Length

433

Subject ID

[gi|157820995|ref|NP_001101539.1|](#)

Description

serine/threonine-protein kinase 11 [Rattus norvegicus] >[gi|149034596|gb|EDL89333.1|](#) serine/threonine kinase 11 (predicted), isoform CRA_a [Rattus norvegicus]

Molecule type

amino acid

Subject Length

436

Program

BLASTP 2.2.24+ [Citation](#)

Reference

Stephen F. Altschul, Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

Reference - compositional score matrix adjustment

Stephen F. Altschul, John C. Wootton, E. Michael Gertz, Richa Agarwala, Aleksandr Morgulis, Alejandro A. Schäffer, and Yi-Kuo Yu (2005) "Protein database searches using compositionally adjusted substitution matrices", FEBS J. 272:5101-5109.

Other reports: [Search Summary](#) [Taxonomy reports](#) [Multiple alignment](#)

[Search Parameters](#)

Search parameter name Search parameter value

Program	blastp
Query range	44-343
Word size	3
Expect value	10
Hitlist size	100
Gapcosts	11,1
Matrix	BLOSUM62

Low Complexity Filter	Yes
Filter string	L;
Genetic Code	1
Window Size	40
Threshold	11
Composition-based stats	2

Karlin-Altschul statistics

Params Ungapped Gapped

Lambda	0.320459	0.267
K	0.139595	0.041
H	0.429592	0.14

Results Statistics

Results Statistics parameter name Results Statistics parameter value

Effective search space	110297
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Graphic Summary**Distribution of Blast Hits on the Query Sequence****[?]**

An overview of the database sequences aligned to the query sequence is shown. The score of each alignment is indicated by one of five different colors, which divides the range of scores into five groups. Multiple alignments on the same database sequence are connected by a striped line. Mousing over a hit sequence causes the definition and score to be shown in the window at the top, clicking on a hit sequence takes the user to the associated alignments. New: This graphic is an overview of database sequences aligned to the query sequence. Alignments are color-coded by score, within one of five score ranges. Multiple alignments on the same database sequence are connected by a dashed line. Mousing over an alignment shows the alignment definition and score in the box at the top. Clicking an alignment displays the alignment detail.

[Dot Matrix View](#)**Plot of lcl|17777 vs gi|157820995|ref|NP_001101539.1| [?]**

This dot matrix view shows regions of similarity based upon the BLAST results. The query sequence is represented on the X-axis and the numbers represent the bases/residues of the query. The subject is represented on the Y-axis and again the numbers represent the bases/residues of the subject. Alignments are shown in the plot as lines. Plus strand and protein matches are slanted from the bottom left to the upper right corner, minus strand matches are slanted from the upper left to the lower right. The number of lines shown in the plot is the same as the number of alignments found by BLAST.

**Descriptions**

Sequences producing significant alignments:		Score (Bits)	E Value
ref NP_001101539.1 	serine/threonine-protein kinase 11 [Rattus...	<u>525</u>	1e-153

Alignments

>ref|NP_001101539.1| serine/threonine-protein kinase 11 [Rattus norvegicus]
 gb|EDL89333.1| serine/threonine kinase 11 (predicted), isoform CRA_a [Rattus norvegicus]
 Length=436

Score = 525 bits (1351), Expect = 1e-153, Method: Compositional matrix adjust.
 Identities = 287/300 (96%), Positives = 291/300 (97%), Gaps = 0/300 (0%)

Query	44	KLIGKYLMDLLGEGSYGKVKEVLDSETLCRRAVkilkkklrriPNGEANVKKEIQLLR	103
Sbjct	44	KLIGKYLMDLLGEGSYGKVKEVLDSETLCRRAVKILKKKKLRRIPNGEANVKKEIQLLR	103
Query	104	RLRHKNVIQLVDVLYNEEKQKMYMVMEYCVCGMQEMLDSVPEKRFPVCQAHGYFCQLIDG	163
Sbjct	104	RLRHRNVIQLVDVLYNEEKQKMYMVMEYCVCGMQEMLDSVPEKRFPVCQAHGYFRQLIDG	163
Query	164	LEYLHSQGIVHKDIKPgnlllttggtlKISDLGVAEALHPFAADDTCRTSQGSPAFQPPE	223
Sbjct	164	LEYLHSQGIVHKDIKPGNLLLTNGTLKISDLGVAEALHPFAVDDTCRTSQGSPAFQPPE	223
Query	224	IANGLDTFSGFKVDIWSAGVTLYNITTGLYPFEGDNIYKLFENIGKGSYAIPGDCGPPLS	283
Sbjct	224	IANGLDTFSGFKVDIWSAGVTLYNITTGLYPFEGDNIYKLFENIG+G + IP DC PPLS	283
Query	284	DLLKGMLEYEPAKRFSIRQIRQHSWFRKKHppaeapvpippspDTKDRWSMTVVPYLED	343
Sbjct	284	DLLRGMLEYEPAKRFSIRQIRQHSWFRKKHPLAEALVPIPPSPDTKDRWSMTVVPYLED	343